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Milk Consumption and Prostate Cancer: A Systematic Review

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Prostate cancer is the third most common cancer in men globally, and the most common cancer among men in the United States. Dietary choices may play an important role in developing prostate cancer; in particular, a higher dairy product intake has been associated with an increased risk of developing prostate cancer. The overall positive association between milk consumption and the risk of prostate cancer development and prostate cancer mortality has been well documented in multiple epidemiological studies. However, there is limited literature on the association between types of milk, as classified by fat content (skim, low fat, and whole), and the risk of developing prostate cancer. When further examining current state of the literature on this topic, there is a number of epidemiologic studies assessing the relationship between prostate cancer and milk consumption. On the contrary, very few experimental studies explore this topic. Further experimental research may be necessary to examine the relationship between dairy and dairy products consumption and the increased risk of development of prostate cancer. At this time, there are no formal clinical recommendations regarding dairy products consumption for patients who are at risk of prostate cancer development or who have a history of prostate cancer. In this manuscript, we sought to systematically review the existing literature on the association between milk consumption classified by fat content, and the risk of developing prostate cancer. These findings may be useful for the clinicians who provide recommendations for the patients at risk of developing prostate cancer.

Keywords: Carcinogenesis; Diet, cariogenic; Diet, western; Prostatic neoplasms

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INTRODUCTION

Despite treatment advances, prostate cancer related mortality rates remain high in the United States. While surgical treatments may play a significant role in reducing a disease progression, prostatectomy may not significantly decrease the mortality related to a localized prostate cancer when compared to an observational approach [1]. Global cancer incidence estimates

reveal that, prostate cancer has become the third most common cancer in men, and half a million new cases are being reported every year [2]. The global burden of prostate cancer is going to be 1.7 million new cases by 2030 [3]. According to the Center for Disease Control, prostate cancer is the most common cancer among men in the United States and one of the leading causes of cancer deaths among men of all races. Prostate cancer mostly occurs in the elderly people with three quarters

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of the cases occurring in men who are above 65 years of age, which is suggestive of the fact that, developed countries having a higher proportion of elderly population report a higher incidence rate of prostate cancer ($\approx 15\%$), compared to the developing countries [2]. Incidence rates in the developing countries are continuing to increase, while mortality rates are staying at a relatively stable level [4].

A review of prostate cancer incidence data from 42 countries suggested that there may be a correlation ($r=0.711$) between milk consumption and prostate cancer incidence [5]. It has been observed that total dairy product intake and calcium from the dairy products has been positively associated with the risk of developing prostate cancer and it was observed that the low fat milk intake was associated with greater risk of non-aggressive form of the disease and whole milk was associated with greater risk of fatal prostate cancer [6]. The association between the risk of developing prostate cancer and dairy products has been linked to the fact that dairy products raise the concentrations of insulin like growth factors [7]. The high fat content in the dairy products has been associated with c-peptide concentration which leads to development of aggressive form of prostate cancer [8]. Metanalysis conducted by Lu and colleagues [9] suggested that increased whole milk consumption may contribute to higher prostate cancer mortality rate (2016). Another metanalysis suggested that high intake of whole milk and low fat milk may contribute to an increased risk to develop prostate cancer [10]. A study of Swedish men suggested that there is an association between whole milk consumption and cancer progression; also, this study suggested that low-fat milk intake may reduce mortality in patients with localized prostate cancer [11]. While the data suggesting that whole milk may contribute to prostate cancer development may appear rather convincing, the effects of skim and low-fat milk are not clear.

There is an abundance of epidemiologic and ecologic studies exploring the relation between prostate cancer and milk consumption. Conversely, only a small number of experimental studies has been conducted to further explore this topic. Prostate cancer development may be affected by estrogen levels [12]. It has been suggested that drinking milk may result in increase of estrone and progesterone levels in the blood [13]. Some authors speculated that modern methods of commercial milk production result in higher level of estrogen

in the milk, which in turn may result in higher rates of prostate and other cancers [14]. Estrogen is not the only compound found in the milk that may affect the development of prostate cancer. One study suggested that milk protein casein may stimulate the proliferation of prostate cancer cells [15].

There is evidence that milk may reduce the risk to develop certain other cancers. For instance, participation in school milk programs has been associated with a reduced risk for developing colorectal cancer [16]. Milk provides essential amino acids, vitamins, and calcium. It is still considered an integral part of healthy diet worldwide. Milk consumption may have certain health benefits and clinical recommendation to eliminate milk from the diet completely may not be feasible. Currently, no structured clinical recommendations exist regarding milk products consumption that may affect the risk of prostate cancer development. There were several reviews of a similar nature conducted in the past [10,17-19]. However, the reviews mentioned above did not focus specifically on milk; they had broader focus, examining the relations of prostate cancer to dietary intake in general, dairy products, or vitamin D consumption. None of the reviews above focused on examining the relationship between fat content in milk and the risk for prostate cancer. To add to that notion, we attempted to create a comprehensive systematic review including all of the current evidence on the topic published in May 2020 or prior. For that reason, we examined the existing literature to explore this topic and provide recommendations for the clinicians who deal with at risk populations.

MATERIALS AND METHODS

1. Search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Review and Metanalysis (PRISMA) guidelines. Literature search was performed by two independent reviewers using PubMed (1982 to May, 2020), Cumulative Index to Nursing and Allied Health Literature (CINAHL; 1982 to May, 2020) (Fig. 1). The search was conducted using free text search terms 'prostate cancer', 'prostate cancer risk', 'milk', 'milk consumption', 'dairy', and 'dairy consumption'. Hand searches of references of other review articles were conducted by the reviewers indepen-

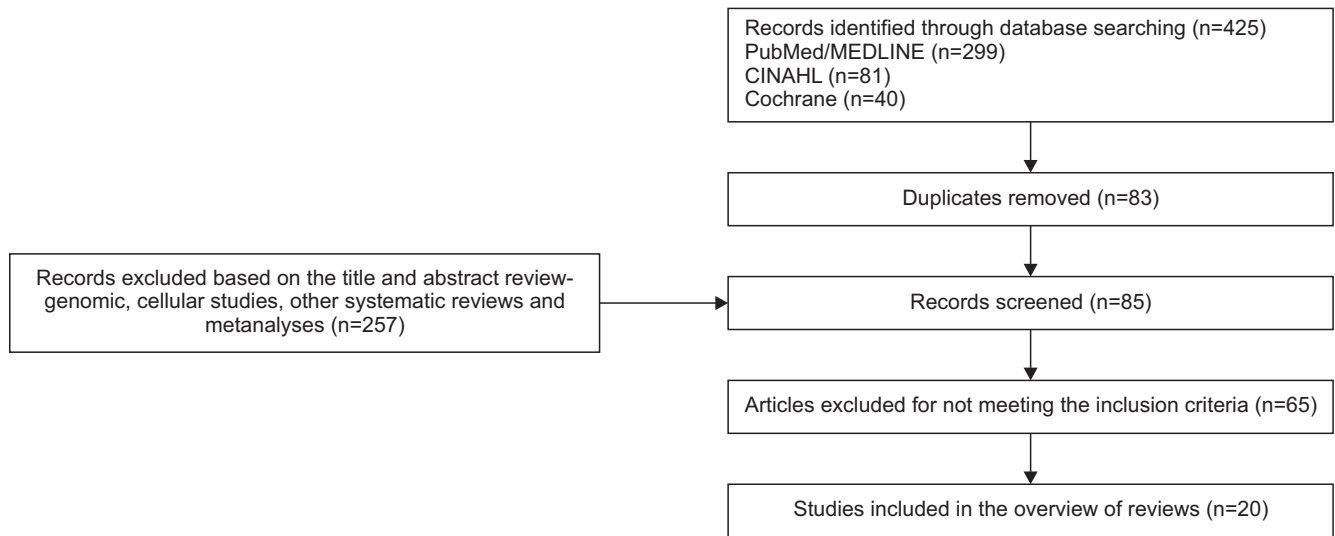


Fig. 1. Systematic review procedure.

dently (Table 1) [5,11,20-36].

2. Screening and data abstraction

Titles and abstracts were screened independently by the two researchers. If the inclusion criteria were met, then the full article was studied. Any disagreement about the inclusion of the articles was resolved by consensus. Information on the author, year of the study, geographical location of the study, type of the study design, study participants, number of the study participants, results and associations found (if any) were collected.

3. Study selection

For selection of the articles, the articles had to be in English and full text articles from 1981 to May 2020. All studies whether they showed a significant association or no association between milk consumption and risk of prostate cancer were included. For the study of association, articles were included, if they presented estimates of risk ratios, hazard ratios, or odds ratios. Studies which mentioned the association of dietary practices were included if they comprised milk consumption. Other systematic reviews, meta-analyses, articles that studied the effects of plant-based milk products, genomic studies and the articles which had titles suggestive of dealing with subjects unrelated to the search were excluded. Authors utilised the above approach to include only the original studies that evaluate the relationship between prostate cancer and milk consumption. Included were addressing the pros-

tate cancer risk (incidence and prevalence) in relation to milk consumption or dairy consumption in general. Selected studies were assessed for risk of bias using The Cochrane Collaboration's tool for assessing risk of bias in randomized trials [37]. All of the studies were considered having a low risk for bias after utilising the above tool.

Authors proceeded with implementing a systematic review of the selected studies because of the heterogeneity of the data in the articles, because of the heterogeneity of the data the implementation of the meta-analysis of the selected studies would not be possible.

RESULTS

There were 20 significant studies which were included in the systematic review. Three of the studies were ecological studies. One of the ecological studies compared the prostate cancer mortality rates in 1986 from 41 countries with the macronutrient supply values for 1983. In the second ecological study, cancer incidence and mortality data from 42 countries were compared with the dietary practices akin to each country. In the third ecological study, age standardized cancer mortality rates from 71 countries were compared with the food consumption data. There were 7 prospective cohort studies and 8 case control studies. Most of the studies that were incorporated were from the United States. Most of the food questionnaires were self-administered questionnaire except the ecological studies where data on food consumption for the countries involved in the

Table 1. Characteristics of the studies involved in the systematic review

Author/study year/country	Study population/ data derived from	Study design and size	Method of data collection for exposure assessment	Exposure (outcome association and main results)
Park et al (2007) [22]/1995–2001/USA	Members of American Association of Retired Persons: 50–71 years	Cohort study 293,888 men	Food frequency questionnaire	Skim milk consumption associated with increased risk of advanced prostate cancer (≥ 2 vs. 0 servings/d: relative risk [RR]=1.23, 95% confidence interval [CI]=0.99–1.54; p [trend]=0.01), stronger association after adjustment for calcium or vitamin D
Grant (1999) [23]/ study year not mentioned/ecological study	Mortality data from 1986 for various age groups in 41 countries	Ecological study Mortality data from 41 countries compared	Mortality data from 1986 for various age groups in 41 countries compared with national consumer macronutrient supply values for 1983 and tomato supply values for 1985	Non-fat portion of milk considered a risk factor for prostate cancer and associated with prostate cancer mortality rates ($R^2=0.73$, $p<0.001$ for men aged 65–74 years)
Ambrosini et al (2008) [27]/2001–2002/Western Australia	Incident prostate cancer cases identified from the West Australian Cancer registry, controls randomly selected among men aged 45–75 with no history of prostate cancer identified through the registry	Case-control study 546 cases and 447 controls	Self-administered questionnaire	An increased risk of prostate cancer associated with western diet with men in highest quartile for western pattern ^a score had an odds ratio (OR) of 1.82 (95% CI=1.15–2.87, $p=0.02$)
Park et al (2007) [20]/1993–1996/ USA	Multiethnic cohort of adult men and women (age 45–75 years) living in Hawaii and California	Cohort study 82,483 men	Self-administered questionnaire	Significant increase in the risk of total prostate cancer for low-/non-fat milk (for the highest [≥ 243 g] vs. the lowest [0 g] quintile was observed with a RR=1.16, 95% CI=1.04–1.29; p [trend]=0.02), significant association also found with localized prostate cancer
Downer et al (2017) [11]/1991–2011/Sweden	Cohort of prostate cancer patients from a case-control study in Örebro County, Sweden	Cohort study 525 prostate cancer patients	Self-administered questionnaire and a 68-item food frequency questionnaire	Total dairy intake (≥ 6 vs. < 3 servings/d) among 525 cases not associated with increased prostate cancer mortality (1.34, 0.86–2.09, p -trend=0.23) High-fat milk intake (≥ 3 vs. < 1 servings/d) was associated with increased prostate cancer mortality (4.86, 1.52–15.57, p -trend=0.03), in 230 men with localized prostate cancer
Bosetti et al (2004) [31]/1991–2002/Italy	Cases were men below 75 years with incident, histologically confirmed prostate cancer patients admitted to the teaching and general hospitals in Italy, between 1991–2002, and controls were men below 75 years admitted due to reasons other than prostate cancer	Case-control study 1,294 cases and 1,451 controls	Self-administered questionnaire on diet	Increased risk of prostate cancer with increased consumption of milk and dairy products, with an OR=1.2 for highest vs. lowest quintile for the frequency of milk and dairy product consumption

study were collected and in one ecological study, national consumer macronutrient supply data were collected. Most of the studies focused on the milk and its association with the risk of prostate cancer while some

studies included other dairy products.

1. Skim milk

Park and colleagues [22] found an association be-

Table 1. Continued 1

Author/study year/country	Study population/ data derived from	Study design and size	Method of data collection for exposure assessment	Exposure (outcome association and main results)
Deneo-Pellegrini et al (2012) [26]/1996–2004/Uruguay	Cases were men aged 40–89 years with incident and histologically confirmed prostatic adenocarcinomas from Uruguay (4 major hospitals in Montevideo), between 1996 and 2004, and controls were patients with no history of smoking/drinking/dietary changes	Case-control study 326 cases and 652 controls	Socio-demographic variables and other risk factors questionnaire and 64-item food frequency questionnaire	Whole milk is positively associated with the risk of prostate cancer with an OR=2.01: 95% CI=1.42–2.82, p-trend≤0.0001
Slattery et al (1990) [28]/January 1, 1984–November 15, 1985/Utah	Cases being white males, 45–75 years with histologically confirmed first primary prostate cancer, controls men above 65 years identified by random dialing (from four urban counties of Utah, between 1984–1985)	Case-control 468 identified as cases of which, 362 completed the interview 891 control subjects identified of which 685 completed interviews	Self-administered questionnaire about adolescent diet, adolescent years, medical and family history and adult dietary intake	Increased prostate cancer risk associated with consuming high saturated fat, diet which includes whole milk, in adults with an OR=1.8, as compared to a lesser risk in adolescents (OR=1.2) and no major differences in risk observed in men aged 45–67 years, 68–74 years for aggressive tumors
Ganmaa et al (2002) [5]/1988–1992/ecological study (data collected from 42 countries)	The incidence and mortality rates of testicular and prostatic cancers in 42 countries were correlated with the dietary practices in these countries using the cancer rates (1988–1992)	Ecological data Cancer incidence data and mortality data and dietary practices from 42 countries	“Cancer incidence in five continents” edited by Parkin et al [2]: cancer incidence data (GLOBOCAN: data on the mortality of testicular and prostate cancers. The consumption data for various food items: FAOSTAT [Food and Agricultural Data] dataset)	Milk was found to be correlated with mortality of prostate cancer (Correlation coefficient, r=0.766), milk+cheese contributed significantly to mortality from prostate cancer (r=0.580)
Colli and Colli (2006) [32]/ecological study (data collected from 71 countries)	Age adjusted cancer rates from the International agency for Research on Cancer (2000) and food consumption data (1990–1992), provided by the Food and Agricultural Organization (FAO) of the United Nations were compared	Ecological study Cancer mortality and food consumption rates obtained from 71 countries	Age standardized cancer mortality rates for 71 countries (GLOBOCAN 2000 database and per capita food intake rates from the food consumption data provided by the FAO of the United Nations)	Correlation found between increased prostate cancer mortality and consumption of total animal calories, total animal fat calories, meat, animal fat, milk (R=0.57), sugar, alcoholic beverages and stimulants
Torniainen et al (2007) [21]/2001–2003/Sweden and Finland	Swedish Study population (Cancer Prostate in Sweden [CAPS] 1 and 2) and Finnish Study population: DNA samples from prostate cancer patients (Tampere University Hospital and the Blood Center of the Finish Red Cross, Tampere)	Case control study Sweden: CAPS Part 1- by 1,352 cases and 858 controls CAPS Part 2-1,524 cases and 963 controls Finland: 1,229 cases and 473 controls	Self-administered questionnaire	High intake of low-fat milk (3 or more glasses of low fat milk vs. no consumption at all) was associated with an increased risk of prostate cancer in the CAPS 1 study, and the adjusted OR was 1.8 (95% CI=1.17–2.9, p-trend=0.003) for advanced cases and 1.5 (95% CI=0.98–2.3, p-trend=0.01) for localized cases

Table 1. Continued 2

Author/study year/country	Study population/ data derived from	Study design and size	Method of data collection for exposure assessment	Exposure (outcome association and main results)
De Stefani et al (1995) [33]/ January 1998–December 1994/Uruguay	Patients admitted to the Instituto Nacional de Oncologia, between January 1988 to December 1994, with cases being men with histologically confirmed prostate cancer and controls were patients with different neoplastic and non-neoplastic conditions	Case control 156 cases and 302 controls	Routine interviews	Increased risk of prostate cancer was associated with beer drinking, meat, milk (odds of 1.3–1.7 with increased frequency) and fruit consumption after adjusting for major confounders
Mettlin et al (1990) [25]/1982–1990/Roswell Park Memorial Institute (RPMI) (New York, USA)	Study participants were patients entering RPMI (New York, USA)	Case control 3,334 cases and 1,300 controls	Questionnaire (number of glasses of whole milk, 2% milk, and skim milk he/she drank each day)	Increases in risk associated with more frequent consumption of whole milk for every cancer site except prostate and uterus OR=1.5 for whole milk OR=1.0 for 2% milk OR=1.2 for skim milk
Talamini et al (1986) [36]/January 1980 and March 1983/ Italy	Cases were men admitted to Oncological Department General hospital of Pordenone, Italy; or referred for follow-up to outpatient clinics, with histologically confirmed diagnosis of prostatic cancer, and controls were men admitted for acute conditions	Case control 166 cases and 202 controls	Questionnaire on socio-demographic factors, general lifestyle habits and selected indicators of nutrition and diet	There was a significant positive relation with milk or cheese consumption and risk of prostate cancer (RR=2.5, 95% CI=1.3–4.7)
Torfadottir et al (2012) [34]/1967 to 1987 through 2009/Iceland	Study participants were from the Reykjavik AGES (Age, Gender, Environmental Susceptibility) study which was a population-based cohort study, initiated by the Icelandic Heart Association in 1967	Prospective cohort study 2,268 participants	Food frequency questionnaire and questions on dietary habits in early life (14–19 years), midlife (40–50 years), and the present time	Effects of high milk intake (at least once a day) vs. less than daily intake Early life: more likely to be diagnosed with prostate cancer, OR=1.58 Adolescent life: 3-fold increase in the risk of advanced prostate cancer (age adjusted model), OR=3.22 (multivariate model) Midlife: no association observed
Giovannucci et al (2006) [8]/1986–January 31, 2002/ USA	A health professional follow-up (followed till January 31, 2002) cohort study was formed in 1986 comprising of 51,529 United States male health professionals (predominantly Caucasian, 40–75 years) who completed a mailed questionnaire	Prospective cohort study 51,529 United States male physicians	Baseline questionnaire and food frequency questionnaire	Positive association seen for calcium, but dairy products were not significantly associated with advanced and fatal prostate cancer risk
Tat et al (2018) [24]/2004–2016/USA	Study was conducted among men enrolled in Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE); an active registry initiated in 1995 that includes 15,000 men with varying stages of biopsy-proven adenocarcinoma	Prospective cohort study 1,334 men	Food frequency questionnaire and questions on post-diagnostic dairy intake included frequency of consumption of dairy foods	Whole milk consumption (>4 servings/wk of whole milk vs. ≤3 servings/mo) seen to be associated with increased risk of prostate cancer recurrence with a hazard ratio (HR)=1.73, p-trend=0.04, attenuated results observed (HR=1.66), after adding saturated fat to the multivariate model

tween skim milk and risk of advanced prostate cancer. While the association was statistically significant, authors discussed that this may have occurred by chance.

Other milk or dairy products consumption had no association with the increased risk for prostate cancer in this study [22]. A study by Grant [23] suggested that

Table 1. Continued 3

Author/study year/country	Study population/ data derived from	Study design and size	Method of data collection for exposure assessment	Exposure (outcome association and main results)
Pal et al (2019) [30]/initiated in 2011, cases identified between (1st January 2010– June 30, 2014)/ Australia	Cases were men below 75 years, diagnosed with advanced prostate cancer from the Victorian Cancer Registry and controls were men below 75 years with prostate specific antigen levels above age specific limits and prostate cancer excluded by biopsy	Case control study 1,254 cases and 818 controls	Food frequency questionnaire	Weak inverse association observed for overall milk intake (highest vs. lowest OR=0.72, 95% CI=0.54–0.98, p-trend=0.058 (model adjusted for covariates like age, socioeconomic status, but unadjusted for trouser size)
Nilsson et al (2020) [36]/ cohorts initiated in mid 80's/Sweden	The study is derived from the Northern Sweden Diet Database (NSDD). First sampling event in NSDD (January 1, 1986 to December 31, 2016) was chosen for this study	Prospective cohort study 105,891 subjects	Food frequency questionnaire: two versions (84 items, 64–66 items)	Consumption of fermented milk associated with increased prostate cancer risk compared to subjects in lowest quintile vs. highest quintile with HR Q5 (highest quintile)–Q1 (lowest quintile)=1.16, 95% CI=1.02–1.32
Steck et al (2018) [29]/study year not mentioned/ USA	This study used data from Prostate Cancer Project Study participants were men aged 40–79 years, Louisiana and North Carolina residents with a histologically confirmed adenocarcinoma of the prostate	Case only study 2,060 participants	Diet history questionnaire	Men who reported higher consumption of whole-fat milk (≥ 1.23 servings/d) had an increased odds of aggressive prostate cancer (OR=1.74; 95% CI=1.16–2.62), as compared to non-whole-fat milk drinkers (fully adjusted model), attenuated association seen, after adjusting for other dietary variables. No association observed with dairy product intake

^aWestern pattern score: high intake of red processed meats, fried fish, hamburgers, chips, high-fat milk, and white bread.

consumption of skim milk and non-fat portion of milk may have high association with prostate cancer incidence. In contrast to these findings other studies examining the association between skim milk consumption and risk for prostate cancer did not suggest such an association [24,25].

2. Whole milk/high-fat milk

In one study men diagnosed with localized prostate cancer, high fat milk consumption was associated with increased prostate cancer-specific mortality while in men with advanced prostate cancer this association was not observed [11]. Whole milk was seen to be positively associated with prostate cancer risk in one study [26]. Increased odds of prostate cancer with whole milk consumption were suggested in a study [25]. A case control study was conducted in Australia to investigate the dietary patterns associated with prostate cancer risk, it was observed that the western pattern diet, which includes high-fat milk was associated with increased odds of prostate cancer risk [27].

In another study the subjects were categorized into

adolescents, young adults and older adults in an attempt to study the food consumption trends and the subsequent prostate cancer risk in different groups. It was observed that there was an increased prostate cancer risk in adolescents consuming fatty foods (includes whole milk), while no significant risk was observed in adults and males aged 45–74 for aggressive tumors [28]. The odds of prostate cancer risk were 1.5 times in men who consumed whole milk as compared to men who consumed 2% milk or skim milk in a study [25]. Higher risk associated with recurrence of prostate cancer was observed in men who consumed whole milk [24]. Another study suggested that male patients who consume whole milk daily have a 74% increased chance of high-aggressive prostate cancer compared to the patients who drink lower fat content or skim milk [29]. Contrary to those findings, a study conducted in Australia suggested that dairy and milk consumption may have an inverse association with the development of advanced prostate cancer [30].

3. Milk (skim or whole milk)

There were some other studies conducted in which the effect of milk on the risk of developing prostate cancer, rather than the skim or whole milk was investigated. In one study by Bosetti and colleagues [31] the researchers observed an increased prostate cancer risk with frequent consumption of milk and dairy products. In an ecological study examining the association between world dietary practices and incidence and mortality of prostate and testicular cancers, a diet rich in milk and cheese contributed to increased prostate cancer mortality rates [14]. In yet another ecological study a strong positive correlation was found between milk consumption and increased prostate cancer mortality [32]. Increased odds of developing prostate cancer with increased consumption of milk was observed in one study [33]. In another study though the study showed an increased odds of developing prostate cancer with increased consumption of milk, the intake of milk in midlife was neither associated with risk of prostate cancer nor advanced prostate cancer [34]. There was a positive relation between prostate cancer risk and milk or cheese consumption in one of the studies [35]. No association was observed between dairy products and risk of advanced or fatal prostate cancer [8]. Conversely, one large, prospective, population-based cohort study conducted in a Northern Sweden population failed to find an association between prostate cancer development and non-fermented or fermented milk consumption regardless of fat content [36]. Another study conducted in the United States suggested that there may be an association between 2% fat milk consumption and advanced prostate cancer, although the authors in this study suggested that this association may have occurred by chance.

DISCUSSION

The overwhelming majority of the studies included in this systematic review were suggestive of a link between milk consumption and increased risk of developing prostate cancer. Only one of the studies in this review did not show an association between milk consumption and increased risk for development of prostate cancer [34]. After conducting this systematic review, it is still unclear that the increased risk for prostate cancer is related to the dietary fat in the milk or non-fat components of the milk. While some studies

found correlation between increased risk for prostate cancer and high fat content in the milk, others suggested that the non-fat components of the milk may be associated with the higher risk for the prostate cancer. Milk and dairy product are components of Western diet and it is possible that the increased risk for development of prostate cancer is related not to milk and dairy products in particular, but to overall carcinogenic effects of western diet.

Further research is needed to examine the relationship between dairy and dairy products consumption and the increased risk of development of prostate cancer. Ganmaa and colleagues [5] hypothesized that estrogens in milk may be related to the development of prostate cancer. High estrogen content in cow milk is a consequence of industrialized milk production [38]. While the hypothesis seems plausible, we were not able to find studies that evaluated the estrogen/estradiol content in the milk and its relation to the risk of developing prostate cancer. To add to this notion, there is a growing body of evidence that oestrogens may contribute to the development of prostate cancers [39]. Further research may confirm the estrogen/estradiol content in the dairy is related to the increased risk of prostate cancer or it will reject the hypothesis that high content milk estrogen may affect the risk for the development of prostate cancer. On the other hand, it may be beneficial to focus on non-fat components of the milk to further evaluate the effect of non-fat components on the risk of development of prostate cancer.

CONCLUSIONS

While the research findings are inconclusive clinicians may recommend to the patients who are at higher risk of prostate cancer development to eliminate or reduce the consumption of milk or milk products, especially those with high fat content. Such a decision should be made jointly with the patient and risks, benefits, and limitations of such a dietary approach should be discussed with the patient. If it is decided to eliminate or limit the consumption of milk products patient should be counseled about the appropriate calcium and vitamin D supplementation.

Prostate cancer is a complex disease with multifactorial origins that include, genetics, diet, and environmental influences. The risk reduction of the prostate cancer development may be achieved when all these

causative domains are fully understood and addressed.

Conflict of Interest

The authors have nothing to disclose.

Author Contribution

Conceptualization: all authors. Data curation: all authors. Methodology: all authors. Software: all authors. Validation: all authors. Writing – original draft: all authors. Writing – review & editing: all authors.

REFERENCES

1. Wilt TJ, Brawer MK, Jones KM, Barry MJ, Aronson WJ, Fox S, et al. Radical prostatectomy versus observation for localized prostate cancer. *N Engl J Med* 2012;367:203-13.
2. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer* 2001;37 Suppl 8:S4-66.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893-917.
4. Center MM, Jemal A, Lortet-Tieulent J, Ward E, Ferlay J, Brawley O, et al. International variation in prostate cancer incidence and mortality rates. *Eur Urol* 2012;61:1079-92.
5. Ganmaa D, Li XM, Wang J, Qin LQ, Wang PY, Sato A. Incidence and mortality of testicular and prostatic cancers in relation to world dietary practices. *Int J Cancer* 2002;98:262-7.
6. Song Y, Chavarro JE, Cao Y, Qiu W, Mucci L, Sesso HD, et al. Whole milk intake is associated with prostate cancer-specific mortality among U.S. male physicians. *J Nutr* 2013;143:189-96.
7. McGreevy KM, Hoel BD, Lipsitz SR, Hoel DG. Impact of nutrients on insulin-like growth factor-I, insulin-like growth factor binding protein-3 and their ratio in African American and white males. *Public Health Nutr* 2007;10:97-105.
8. Giovannucci E, Liu Y, Stampfer MJ, Willett WC. A prospective study of calcium intake and incident and fatal prostate cancer. *Cancer Epidemiol Biomarkers Prev* 2006;15:203-10.
9. Lu W, Chen H, Niu Y, Wu H, Xia D, Wu Y. Dairy products intake and cancer mortality risk: a meta-analysis of 11 population-based cohort studies. *Nutr J* 2016;15:91.
10. Aune D, Navarro Rosenblatt DA, Chan DS, Vieira AR, Vieira R, Greenwood DC, et al. Dairy products, calcium, and prostate cancer risk: a systematic review and meta-analysis of cohort studies. *Am J Clin Nutr* 2015;101:87-117.
11. Downer MK, Batista JL, Mucci LA, Stampfer MJ, Epstein MM, Håkansson N, et al. Dairy intake in relation to prostate cancer survival. *Int J Cancer* 2017;140:2060-9.
12. Qin LQ, Wang PY, Kaneko T, Hoshi K, Sato A. Estrogen: one of the risk factors in milk for prostate cancer. *Med Hypotheses* 2004;62:133-42.
13. Maruyama K, Oshima T, Ohyama K. Exposure to exogenous estrogen through intake of commercial milk produced from pregnant cows. *Pediatr Int* 2010;52:33-8.
14. Li XM, Ganmaa D, Qin LQ, Liu XF, Sato A. [The effects of estrogen-like products in milk on prostate and testes]. *Zhonghua Nan Ke Xue* 2003;9:186-90. Chinese.
15. Park SW, Kim JY, Kim YS, Lee SJ, Lee SD, Chung MK. A milk protein, casein, as a proliferation promoting factor in prostate cancer cells. *World J Mens Health* 2014;32:76-82.
16. Cox B, Sneyd MJ. School milk and risk of colorectal cancer: a national case-control study. *Am J Epidemiol* 2011;173:394-403.
17. Harrison S, Lennon R, Holly J, Higgins JPT, Gardner M, Perks C, et al. Does milk intake promote prostate cancer initiation or progression via effects on insulin-like growth factors (IGFs)? A systematic review and meta-analysis. *Cancer Causes Control* 2017;28:497-528.
18. Mandair D, Rossi RE, Pericleous M, Whyand T, Caplin ME. Prostate cancer and the influence of dietary factors and supplements: a systematic review. *Nutr Metab (Lond)* 2014;11:30.
19. Chan JM, Giovannucci EL. Dairy products, calcium, and vitamin D and risk of prostate cancer. *Epidemiol Rev* 2001;23:87-92.
20. Park SY, Murphy SP, Wilkens LR, Stram DO, Henderson BE, Kolonel LN. Calcium, vitamin D, and dairy product intake and prostate cancer risk: the Multiethnic Cohort Study. *Am J Epidemiol* 2007;166:1259-69.
21. Tornaiainen S, Hedelin M, Autio V, Rasinperä H, Bälter KA, Klint A, et al. Lactase persistence, dietary intake of milk, and the risk for prostate cancer in Sweden and Finland. *Cancer Epidemiol Biomarkers Prev* 2007;16:956-61.
22. Park Y, Mitrou PN, Kipnis V, Hollenbeck A, Schatzkin A, Leitzmann MF. Calcium, dairy foods, and risk of incident and fatal prostate cancer: the NIH-AARP Diet and Health Study. *Am J Epidemiol* 2007;166:1270-9.
23. Grant WB. An ecologic study of dietary links to prostate cancer. *Altern Med Rev* 1999;4:162-9.
24. Tat D, Kenfield SA, Cowan JE, Broering JM, Carroll PR, Van Blarigan EL, et al. Milk and other dairy foods in relation to prostate cancer recurrence: data from the cancer of the prostate strategic urologic research endeavor (CaPSURE™). *Prostate* 2018;78:32-9.
25. Mettlin CJ, Schoenfeld ER, Natarajan N. Patterns of milk con-

- sumption and risk of cancer. *Nutr Cancer* 1990;13:89-99.
26. Deneo-Pellegrini H, Ronco AL, De Stefani E, Boffetta P, Correa P, Mendilaharsu M, et al. Food groups and risk of prostate cancer: a case-control study in Uruguay. *Cancer Causes Control* 2012;23:1031-8.
 27. Ambrosini GL, Fritschi L, de Klerk NH, Mackerras D, Leavy J. Dietary patterns identified using factor analysis and prostate cancer risk: a case control study in Western Australia. *Ann Epidemiol* 2008;18:364-70.
 28. Slattery ML, Schumacher MC, West DW, Robison LM, French TK. Food-consumption trends between adolescent and adult years and subsequent risk of prostate cancer. *Am J Clin Nutr* 1990;52:752-7.
 29. Steck SE, Omofuma OO, Su LJ, Maise AA, Woloszynska-Read A, Johnson CS, et al. Calcium, magnesium, and whole-milk intakes and high-aggressive prostate cancer in the North Carolina-Louisiana Prostate Cancer Project (PCaP). *Am J Clin Nutr* 2018;107:799-807.
 30. Pal M, Hodge AM, Papa N, MacInnis RJ, Bassett JK, Bolton D, et al. Body size and dietary risk factors for aggressive prostate cancer: a case-control study. *Cancer Causes Control* 2019;30:1301-12.
 31. Bosetti C, Micelotta S, Dal Maso L, Talamini R, Montella M, Negri E, et al. Food groups and risk of prostate cancer in Italy. *Int J Cancer* 2004;110:424-8.
 32. Colli JL, Colli A. International comparisons of prostate cancer mortality rates with dietary practices and sunlight levels. *Urol Oncol* 2006;24:184-94.
 33. De Stefani E, Fierro L, Barrios E, Ronco A. Tobacco, alcohol, diet and risk of prostate cancer. *Tumori* 1995;81:315-20.
 34. Torfadottir JE, Steingrimsdottir L, Mucci L, Aspelund T, Kasperzyk JL, Olafsson O, et al. Milk intake in early life and risk of advanced prostate cancer. *Am J Epidemiol* 2012;175:144-53.
 35. Talamini R, La Vecchia C, Decarli A, Negri E, Franceschi S. Nutrition, social factors and prostatic cancer in a Northern Italian population. *Br J Cancer* 1986;53:817-21.
 36. Nilsson LM, Winkvist A, Esberg A, Jansson JH, Wennberg P, van Guelpen B, et al. Dairy products and cancer risk in a Northern Sweden population. *Nutr Cancer* 2020;72:409-20.
 37. Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al.; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
 38. Haimov-Kochman R, Shore LS, Laufer N. The milk we drink, food for thought. *Fertil Steril* 2016;106:1310-1.
 39. Bonkhoff H, Berges R. The evolving role of oestrogens and their receptors in the development and progression of prostate cancer. *Eur Urol* 2009;55:533-42.